

#### SEQUENCE LISTING

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gat Asp	ttt Phe 165	ctc Leu	aaa Lys	gag Glu	gag Glu	gaa Glu 170	cat His	gac Asp	tgt Cys	ttc Phe	ttg Leu 175	gaa Glu	gag Glu	ata Ile	atg Met		584
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tca a Ser I																1448
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Asp Val Leu Glu Ala Lys Met Arq His Gly Phe Ser Gly Ile Pro Ile
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cct Pro	ctg Leu	G1y 999	gtc Val 180	aac Asn	ttg Leu	ggg Gly	aag Lys	aac Asn 185	aag Lys	acc Thr	tca Ser	gtg Vai	gac Asp 190	gcc Ala	gcg Ala	576
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<302> Recombinant human Dinydroorotate Denydrogenase
<303> Arch. Biochem. Biophys. (1995)
<304> 323
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<301> Davis et al.
<302> Histidine to Alanine mutants of Human Dihydroorota
<303> Biochem. Pharmacol. (1997)
<304> 54
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Val Val Lys Glu Leu Gly Ile Asp Gly Leu Ile Val Thr Asn Thr Thr
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Gly Leu Ser Gly Lys Pro Leu Arg Asp Leu Ser Thr Gln Thr Ile Arg
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Glu Met Tyr Ala Leu Thr Gln Gly Arg Val Pro Ile Ile Gly Val Gly
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Gly Val Ser Ser Gly Gln Asp Ala Leu Glu Lys Ile Arg Ala Gly Ala
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Ser Leu Val Gln Leu Tyr Thr Ala Leu Thr Phe Trp Gly Pro Pro Val
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Val Gly Lys Val Lys Arg Glu Leu Glu Ala Leu Leu Lys Glu Gln Gly
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Leu Gly Gly Cys Arg Arg Leu Pro Leu Thr Cys Arg Gln Leu Arg Phe
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                                  25
gcc tcc gac agc gga gcc gca gcg gca act aca aaa gca acg gcc gaa
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Ala Ser Asp Ser Gly Ala Ala Ala Ala Thr Thr Lys Ala Thr Ala Glu
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         35
                                                                       192
tca qca qcc qaq tca qct aqt ata aac gtc aaa gag gca ccc aaa aag
Ser Ala Ala Glu Ser Ala Ser Ile Asn Val Lys Glu Ala Pro Lys Lys
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                                                                       240
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Ala Gly Arg Gly Leu Arg Arg Thr Val Leu Gly Thr Ser Leu Ala Leu
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acg ctg ctg gtt gga tat gtc tac ggg acg gac acc cgg gcg agt gtg
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Thr Leu Leu Val Gly Tyr Val Tyr Gly Thr Asp Thr Arg Ala Ser Val
                                                           95
cat cgg tac ggt gtt gtg ccg ctg att aga gca ttg tat cct gat gcg
                                                                       336
His Arg Tyr Gly Val Val Pro Leu Ile Arg Ala Leu Tyr Pro Asp Ala
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            100
gaa gat gcg cat cat att ggt gtc gat act tta aag atg ctg tat aag
                                                                       384
Glu Asp Ala His His Ile Gly Val Asp Thr Leu Lys Met Leu Tyr Lys
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120

115

						gaa Glu 135						_			_	432	
						Gly 999										480	
						cat His										528	
			_		_	gaa Glu	_		_						_	576	
						cgc Arg							_		_	624	
						ctc Leu 215									_	672	
_		_			_	gta Val										720	
					_	aag Lys			_				_	_	_	768	
				_		cag Gln								_	_	816	
_	_		_	_		cct Pro	-		_		_	_				864	
_						gac Asp 295	_		_							912	
_			_	_	_	ccc Pro						_	_			960	
_		_	_			gct Ala		_	_	_	_	_		_	_	1008	
_	-			-	_	acc Thr				_						1056	
	_	_	_		_	gaa Glu		_						_	_	1104	
_	_			_	_	gga Gly 375			_							1152	

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cgc Arg	aca Thr	gtg Val	gcc Ala 420	ctt Leu	gtg Val	gct Ala	cgg Arg	tac Tyr 425	cgc Arg	tcc Ser	atg Met	ctg Leu	gat Asp 430	gcg Ala	gag Glu	1296
tcg Ser	gaa Glu	acg Thr 435	gcc Ala	gga Gly	tcc Ser	gcc Ala	aag Lys 440	gat Asp	tca Ser	gca Ala	gcg Ala	acc Thr 445	ata Ile	gcg Ala	caa Gln	1344
						aac Asn 455										1392
						ttc Phe										1440
						gac Asp										1488
acc Thr	ggt Gly	gtg Val	gtc Val 500	tat Tyr	ggt Gly	ggc Gly	gtc Val	ggc Gly 505	act Thr	gtc Val	act Thr	cga Arg	gtg Val 510	aag Lys	caa Gln	1536
_		_				aag Lys	_									1560
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	)> 26		7	0	Dha	7	Ta	Tou	Thr	Dho	Cor	Clar	ח [ ת	Sar	λνα	
1				5		Arg			10					15		
	_	_	20			Leu		25					30			
		35				Ala	40					45				
	50					Ser 55					60					
65					70	Arg				75					80	
				85		Val Pro			90					95		
	_	_	100					105					110			
	_	115				Gly	120					125				
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Ile Gly Pro Ala Ile Val Glu Val Gly Gly Thr Thr Pro Leu Pro Gln
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 Asp Gly Asn Pro Arg Pro Arg Glu Phe Arg Leu Pro Ser Gln Arg Ala
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 Met Ile Asn Arg Tyr Gly Leu Asn Ser Lys Gly Ala Asp His Met Ala
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 Ala Ile Leu Glu Gln Arg Val Arg Asp Phe Ala Tyr Ala Asn Gly Phe
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 225
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 Gly Ala Tyr Asp Ala Ala Lys Gln Arg Val Leu Asp Gly Glu Ala Gly
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Val Pro Pro Gly Ser Leu Gln Pro Gly Lys Leu Leu Ala Val Gln Val
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Ala Lys Asn Lys Ala Thr Pro Asp Gly Asp Ile Glu Ala Ile Lys Arg
Asp Tyr Val Tyr Cys Val Asp Arg Val Ala Lys Tyr Ala Asp Ile Leu
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                         295
Val Val Asn Val Ser Ser Pro Asn Thr Pro Gly Leu Arg Asp Leu Gln
                     310
 Ala Thr Ala Pro Leu Thr Ala Ile Leu Ser Ala Val Val Gly Ala Ala
                                                           335
                                      330
 Lys ser val Ash Arg Lys Thr Lys Pro Tyr val Met val Lys val Ser
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 Pro Asp Glu Asp Ser Asp Glu Gln Val Ser Gly Ile Cys Asp Ala Val
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 Arg Ala Ser Gly Val Asp Gly Val Ile Val Gly Asn Thr Thr Asn Arg
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 Arg Pro Asp Pro Ile Pro Gln Gly Tyr Thr Leu Pro Ala Lys Glu Gln
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 Ala Thr Leu Lys Glu Thr Gly Gly Tyr Ser Gly Pro Gln Leu Phe Asp
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 Arg Thr Val Ala Leu Val Ala Arg Tyr Arg Ser Met Leu Asp Ala Glu
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 Ser Glu Thr Ala Gly Ser Ala Lys Asp Ser Ala Ala Thr Ile Ala Gln
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 Thr Glu Pro Gly Ser Glu Asn Val Pro Pro Val Glu Ala Pro Ser Gly
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 Leu Pro Arg Lys Val Ile Phe Ala Ser Gly Gly Ile Thr Asn Gly Lys
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 Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr
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                  5
 ctg ggt ggt tgt cgc cgt ctc cca cta acc tgc aga caa ctt cga ttc
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tca Ser	gca Ala 50	gcc Ala	gag Glu	tca Ser	gct Ala	agt Ser 55	ata Ile	aac Asn	gtc Val	aaa Lys	gag Glu 60	gca Ala	ccc Pro	aaa Lys	aag Lys	1	192
gcc Ala 65	gga Gly	cgg Arg	ggc Gly	ctg Leu	cgg Arg 70	cgc Arg	acg Thr	gtc Val	ctg Leu	gga Gly 75	acg Thr	tcg Ser	ttg Leu	gcg Ala	ctg Leu 80	2	240
acg Thr	ctg Leu	ctg Leu	gtt Val	gga Gly 85	tat Tyr	gtc Val	tac Tyr	G1 999	acg Thr 90	gac Asp	acc Thr	cgg Arg	gcg Ala	agt Ser 95	gtg Val	2	288
cat	cgg	tac	ggt	gtt	gtg	ccg	ctg	att	aga	gca	ttg	tat	cct	gat	gcg	3	336
 his	Arg	тут	Gly 100	val	vai	Pro	Leu	11e 105	Arg	AIä	Leu	Tyr	Pro 110	Asp	Ala		
gaa Glu	gat Asp	gtg Val 115	cat His	cat His	att Ile	ggt Gly	gtc Val 120	gat Asp	act Thr	tta Leu	aag Lys	atg Met 125	ctg Leu	tat Tyr	aag Lys	3	384
tat Tyr	ggt Gly 130	ctg Leu	cat His	cca Pro	agg Arg	gaa Glu 135	cgg Arg	Gly 999	gat Asp	ccg Pro	gat Asp 140	gga Gly	gat Asp	Gly 999	gcg Ala	4	132
			gag Glu													4	180
tcg Ser	ggc Gly	ggc Gly	ctg Leu	gac Asp 165	aag Lys	cat His	gct Ala	gag Glu	atc Ile 170	cct Pro	gat Asp	ccg Pro	ctg Leu	ttc Phe 175	gcg Ala	į	528
atc Ile	ggt Gly	cct Pro	gcc Ala 180	att Ile	gtc Val	gaa Glu	gtc Val	999 Gly 185	ggt Gly	acg Thr	aca Thr	ccc Pro	tta Leu 190	cca Pro	cag Gln	į	576
gat Asp	ggt Gly	aac Asn 195	ccg Pro	cgt Arg	cct Pro	cgc Arg	gta Val 200	ttc Phe	cga Arg	ctt Leu	cca Pro	tca Ser 205	cag Gln	aga Arg	gcg Ala	6	524
atg Met	ata Ile 210	aac Asn	cgg Arg	tac Tyr	ggc Gly	ctc Leu 215	aac Asn	tcc Ser	aaa Lys	ggc Gly	gca Ala 220	gat Asp	cac His	atg Met	gca Ala	•	672
			gag Glu													•	720
gly ggg	gca Ala	tac Tyr	gat Asp	gcg Ala 245	gct Ala	aag Lys	cag Gln	cgt Arg	gta Val 250	ttg Leu	gac Asp	ggc Gly	gaa Glu	gct Ala 255	ggt Gly	,	768
gtg Val	cca Pro	cca Pro	ggt Gly 260	agt Ser	ctt Leu	cag Gln	cct Pro	ggt Gly 265	aag Lys	ctt Leu	tta Leu	gct Ala	gtc Val 270	caa Gln	gtg Val	1	816
gca Ala	aag Lys	aac Asn	aag Lys	gcc Ala	act Thr	cct Pro	gac Asp	ggc Gly	gac Asp	att Ile	gaa Glu	gcc Ala	atc Ile	aag Lys	cgc Arg	,	864

# 24751-2502 275 280 285

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														ctt Leu		96	0
														gcg Ala 335		100	8
														gtc Val		105	6
 ccg Pro	gat Asp	gaa Glu 355	gac Asp	tca Ser	gat Asp	gaa Glu	caa Gln 360	gtc Val	tct Ser	ggt Gly	atc Ile	tgc Cys 365	gac Asp	gcc Ala	gtc Val	110	4
cga Arg	gca Ala 370	tcc	ggt Gly	gtc Val	gac Asp	gga Gly 375	gtg	att Ile	gtc Val	gga Gly	aac Asn 380	aca Thr	aca Thr	aac Asn	cgt Arg	115	2
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gca Ala	acg Thr	ttg Leu	aaa Lys	gaa Glu 405	acc Thr	ggc Gly	gjà aaa	tat Tyr	tca Ser 410	ggt Gly	cca Pro	cag Gln	ctg Leu	ttc Phe 415	gat Asp	124	8
														gcg Ala		129	6
														gcg Ala		134	4
														agc Ser		139	2
														ggg Gly		144	0
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Gln Ala His Ala Val Leu Asp Thr Gly Ala Ser Val Ala Met Met Tyr

470

475

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                                                                       108
       Met Ala Asp Tyr Leu Ile Ser Gly Gly Thr Ser Tyr Val Pro
gac gac ggg ctc aca gcg cag ctc ttc aac tgc ggg gac ggc ctc
                                                                       156
Asp Asp Gly Leu Thr Ala Gln Gln Leu Phe Asn Cys Gly Asp Gly Leu
 15
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                                          25
                                                                       204
acc tac aat gat ttt ctc att ctt cct ggg tat atc gac ttc act gca
Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
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Asp Gln Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys
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                                  55
                                                      60
                                                                       300
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Thr Pro Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met
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                              70
gcc atc gcg atg gcg ctt aca gga ggt att ggt ttc atc cac cac aac
                                                                       348
Ala Ile Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn
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                          85
                                              90
tgc aca cct gaa ttc cag gcc aat gaa gtt cgg aaa gtg aag aaa tac
                                                                       396
Cys Thr Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr
                                                              110
                    100
                                         105
                                                                       444
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Glu Gln Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg
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                115
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gta cgc gat gtt ttt gag gcc aaa gcc agg cat ggc ttc tgt ggt atc
Val Arq Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile
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                                                                       540
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Pro Ile Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile
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Ser Ser Arg Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe
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                                             170
    160
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                                                                       636
Leu Glu Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala
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175
                     180
                                         185
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						gtg Val											732	2
						aag Lys											780	)
•						ctg Leu											828	3
						ctg Leu 260											876	
						tcc Ser											924	1
						gag Glu											972	2
						gcg Ala											1020	)
	gat Asp	gct Ala 320	ttg Leu	cga Arg	gtc Val	ggc Gly	atg Met 325	gga Gly	agt Ser	ggt Gly	tcc Ser	atc Ile 330	tgc Cys	atc Ile	acc Thr	cag Gln	1068	3
	gaa Glu 335	gtg Val	ttg Leu	gcc Ala	tgt Cys	999 Gly 340	cgg Arg	ccc Pro	caa Gln	gcc Ala	aca Thr 345	gca Ala	gtg Val	tac Tyr	aag Lys	gtc Val 350	1116	5
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						cat His											1212	2
						tcc Ser											1260	)
						gat Asp											1308	3
						atg Met 420											1356	5
						aaa Lys											1404	1

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                                                                   1500
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        465
                                                                   1548
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Val Arg Ala Met Thr Tyr Ser Gly Glu Leu Lys Phe Glu Lys Arg Thr
    480
tcc tct gct cag gtg gaa ggt ggc gtc cac agc ctc cat tcg tac gag
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Ser Ser Ala Gln Val Glu Gly Gly Val His Ser Leu His Ser Tyr Glu
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495
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Val Asp Leu Thr Ser Ala Leu Thr Lys Lys Ile Thr Leu Lys Thr Pro
Leu Val Ser Ser Pro Met Asp Thr Val Thr Glu Ala Gly Met Ala Ile
                                                           80
65
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Ala Met Ala Leu Thr Gly Gly Ile Gly Phe Ile His His Asn Cys Thr
Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr Glu Gln
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                               105
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Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg
                           120
        115
Asp Val Phe Glu Ala Lys Ala Arg His Gly Phe Cys Gly Ile Pro Ile
Thr Asp Thr Gly Arg Met Gly Ser Arg Leu Val Gly Ile Ile Ser Ser
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Arq Asp Ile Asp Phe Leu Lys Glu Glu Glu His Asp Arg Phe Leu Glu
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Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala Gly Val
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Thr Leu Lys Glu Ala Asn Glu Ile Leu Gln Arg Ser Lys Lys Gly Lys
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Thr Asp Leu Lys Lys Asn Arg Asp Tyr Pro Leu Ala Ser Lys Asp Ala
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Thr Tyr Asn Asp Phe Leu Ile Leu Pro Gly Tyr Ile Asp Phe Thr Ala
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_	aca Thr		_		_	_		_	_				_			396
_	cag Gln					_		_	_		_		_	_		444
	cgc Arg															492
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	atc Ile														atc Ile	540
	tca Ser 160		_		_			_	_	_					_	588
	gaa Glu														_	636
	gtc Val									_	_	_				684
	aag Lys						_		_		_		_			732
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	gac Asp	_			_	_		_	_		_		_	_		876
	gtt Val	_	_			_	_									924
	aaa Lys				_	_										972
	gta Val	_		_	_		_	_				_	_	_	_	1020

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	c tct r Ser															1596	
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Pro Glu Phe Gln Ala Asn Glu Val Arg Lys Val Lys Lys Tyr Glu Gln
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Gly Phe Ile Thr Asp Pro Val Val Leu Ser Pro Lys Asp Arg Val Arg
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Glu Ile Met Thr Lys Arg Glu Asp Leu Val Val Ala Pro Ala Gly Val
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-54 of 57-

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